



# UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE  
United States Patent and Trademark Office  
Address: COMMISSIONER FOR PATENTS  
P.O. Box 1450  
Alexandria, Virginia 22313-1450  
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/537,320	06/02/2005	Akihiro Tada	TOYA107.007APC	3197
20995 7590 04/06/2011 KNOBBE MARTENS OLSON & BEAR LLP 2040 MAIN STREET FOURTEENTH FLOOR IRVINE, CA 92614				
EXAMINER SZNAIDMAN, MARCOS L				
ART UNIT		PAPER NUMBER		
1628				
NOTIFICATION DATE		DELIVERY MODE		
04/06/2011		ELECTRONIC		

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

jcartee@kmob.com  
efiling@kmob.com  
eOAPilot@kmob.com



UNITED STATES PATENT AND TRADEMARK OFFICE

Commissioner for Patents  
United States Patent and Trademark Office  
P.O. Box 1450  
Alexandria, VA 22313-1450  
[www.uspto.gov](http://www.uspto.gov)

**BEFORE THE BOARD OF PATENT APPEALS  
AND INTERFERENCES**

Application Number: 10/537,320  
Filing Date: June 02, 2005  
Appellant(s): TADA ET AL.

---

Che S. Chereskin  
For Appellant

**EXAMINER'S ANSWER**

This is in response to the appeal brief filed 02/17/2011 appealing from the Office action mailed 10/04/2010.

**(1) Real Party in Interest**

The examiner has no comment on the statement, or lack of statement, identifying by name the real party in interest in the brief.

**(2) Related Appeals and Interferences**

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

**(3) Status of Claims**

The following is a list of claims that are rejected and pending in the application:

Claims 7, 12-14, and 16-17 are pending.

Claims 7, 12-14, and 16-17 are rejected.

**(4) Status of Amendments after Final**

The examiner has no comment on the appellant's statement of the status of amendments after final rejection contained in the brief.

**(5) Summary of Claimed Subject Matter**

The examiner has no comment on the summary of claimed subject matter contained in the brief.

**(6) Grounds of Rejection to be reviewed on Appeal**

The examiner has no comment on the appellant's statement of the grounds of rejection to be reviewed on appeal. Every ground of rejection set forth in the Office action from which the appeal is taken (as modified by any advisory actions) is being maintained by the examiner except for the grounds of rejection (if any) listed under the subheading "WITHDRAWN REJECTIONS." New grounds of rejection (if any) are provided under the subheading "NEW GROUNDS OF REJECTION."

**(7) Claims Appendix**

The examiner has no comment on the copy of the appealed claims contained in the Appendix to the appellant's brief.

**8) Evidence Relied Upon**

The following is a listing of the evidence (e.g., patents, publications, Official Notice, and admitted prior art) relied upon in the rejection of claims under appeal.

EP 1 147 764

Ishida et. al.

10-2001

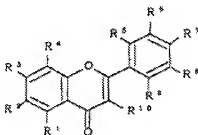
### (9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

#### ***Claim Rejections - 35 USC § 103***

Claims 7, 12-14 and 16-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ishida et. al. (EP 1147764, cited by applicant, cited in prior office action).

For claim 7, Ishida et. al. teach a cosmetic composition of general formula I (see page 3):



, having a sufficient whitening effect, a so called anti skin-aging effect as vitalizing the skin and preventing wrinkles (see page 2, paragraphs [0006] and [0007]). Ishida does not specifically disclose the compound Centaureidin. Ishida et. al. limit their structure to at least four methoxy groups (see page 3, line 18), while Centaureidin has three methoxy groups.

However, MPEP 2144, Section III states: prior art structures do not have to be true homologs or isomers to render structurally similar compounds *prima facie* obvious. *In re Payne*, 606 F.2d 303, 203 USPQ 245 (CCPA 1979) (Claimed and prior art compounds were both directed to heterocyclic carbamoyloximino compounds having

pesticidal activity. The only structural difference between the claimed and prior art was that the ring structures of the claimed compounds had two carbon atoms between two sulfur atoms, whereas the prior art ring structures had either one or three carbon atoms between two sulfur atoms. The court held that although the prior art compounds were not true homologs or isomers of the claimed compounds, the similarity between the chemical structures and properties is sufficiently close that one of ordinary skill in the art would have been motivated to make the claimed compounds in searching for new pesticides). In *re Gyurik*, 201 USPQ 552, 596 F.2d 1012 on page 557 states: "In obviousness rejections based on close similarity in chemical structure, the necessary motivation to make a claimed compound, and thus the *prima facie* case of obviousness, rises from the expectation that compounds similar in structure will have similar properties." In the instant case, it is expected that the compounds of general structure I taught by Ishida et. al., which encompasses analogs of Centaureidin with an extra –OCH<sub>3</sub> group instead of an –OH group, and Centaureidin of the instant application, would have similar chemical, physical and biochemical properties.

The phrase: "whereby elongation of melanocytic dendrites is inhibited" is not given any patentable weight because: the whereby clause represents the intended result of the process steps positively recited. See MPEP 2111.04: In *Hoffer v. Microsoft Corp.*, 405 F.3d 1326, 1329, 74 USPQ2d 1481, 1483 (Fed. Cir. 2005), the court held that when a "whereby" clause states a condition that is material to patentability; it cannot be ignored in order to change the substance of the invention." *Id.* However, the court noted (quoting *Minton v. Nat'l Ass'n of Securities Dealers, Inc.*, 336

F.3d 1373, 1381, 67 USPQ2d 1614, 1620 (Fed. Cir. 2003)) that a “whereby clause in a method claim is not given weight when it simply expresses the intended result of a process step positively recited.” *Id.*

Alternatively, even if one were to give some weight to the phrase: “whereby elongation of melanocytic dendrites is inhibited”, naturally flows from the teachings of the prior art and will necessary be present in the method made obvious by Ishida, since Ishida teaches similar active steps of the instant application: applying compounds close related to Centaureidin to the skin of individuals in need of skin whitening. In other words, products of identical or similar composition cannot exert mutually exclusive properties when administered under the same circumstances. In other words, even though the prior art is silent regarding “*inhibiting elongation of melanocytic dendrites*”, by practicing the method made obvious by the prior art: “*applying compounds like Centaureidin to the skin*”, one will be also be “*inhibiting elongation of melanocytic dendrites*”, even though the prior art was not aware of it. Apparently, Applicant has discovered a new property or advantage of the method made obvious by the prior art. MPEP 2145 II states: “The fact that Applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art, cannot be the basis for patentability when the differences would otherwise be obvious” *Ex parte Obiaya*, 227 USPQ 58, 60.

Since Ishida et. al. teach a method of skin whitening with compounds of formula I (see above), and since Centaureidin, which differs from those compounds by just one methyl group is expected to have similar chemical and biological properties, at the time

of the invention it would have been *prima facie* obvious for a person of ordinary skill in the art to substitute one functional equivalence (a compound of formula I or structurally related to formula I) for another (Centaureidin) with an expectation of success, since the prior art establishes that both function in similar manner, thus resulting in the practice of claim 7, with a reasonable expectation of success.

Claim 12 is a narrower version of claim 7, which insofar recites the same limitations as claim 7, wherein a skin preparation for external use comprising 0.005 to 5% by weight of Centaureidin is applied.

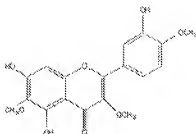
Claim 13, further limits claim 12, wherein the skin preparation for external use is a cosmetic.

For claims 12 and 13, Ishida further teaches: that the cosmetic composition (cosmetic compositions are for external use) of the present invention includes 0.00005 to 10% by weight of the compounds of formula I (see page 2, paragraph [0007]). These percentages clearly overlap with the percentages of the instant claims.

Ishida does not teach the exact same percentages of the instant claims. However, MPEP 2144.05 states: In the case where the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a *prima facie* case of obviousness exists. *In re Wertheim*, 541 F.2d 257, 191 USPQ 90 (CCPA 1976); *In re Woodruff*, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990). Thus resulting in the practice of claims 12-13 with a reasonable expectation of success.

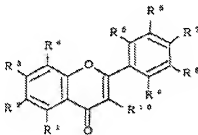


Claim 14 recites a method for treating dyschromatosis (a skin disease in which individuals have anomalous skin pigmentation) comprising: a step of applying Centaureidin represented by the following formula:



and/or a salty thereof to the skin of an individual in need of skin whitening, whereby elongation of melanocytic dendrites is inhibited.

For claim 14, Ishida et. al. teach a cosmetic composition of general formula I (see page 3):



, having a sufficient whitening effect, a so called anti skin-aging effect as vitalizing the skin and preventing wrinkles (see page 2, paragraphs [0006] and [0007]). Ishida does not specifically disclose the compound Centaureidin (Ishida et. al. limit their structure to at least four methoxy groups (see page 3, line 18), while Centaureidin has three methoxy groups) or the specific treatment of dyschromatosis

However, MPEP 2144, Section III states: prior art structures do not have to be true homologs or isomers to render structurally similar compounds *prima facie* obvious. *In re Payne*, 606 F.2d 303, 203 USPQ 245 (CCPA 1979) (Claimed and prior art compounds were both directed to heterocyclic carbamoyloximino compounds having pesticidal activity. The only structural difference between the claimed and prior art was that the ring structures of the claimed compounds had two carbon atoms between two sulfur atoms, whereas the prior art ring structures had either one or three carbon atoms between two sulfur atoms. The court held that although the prior art compounds were not true homologs or isomers of the claimed compounds, the similarity between the chemical structures and properties is sufficiently close that one of ordinary skill in the art would have been motivated to make the claimed compounds in searching for new pesticides). *In re Gyurik*, 201 USPQ 552, 596 F2d 1012 on page 557 states: "In obviousness rejections based on close similarity in chemical structure, the necessary motivation to make a claimed compound, and thus the *prima facie* case of obviousness, rises from the expectation that compounds similar in structure will have similar properties." In the instant case, it is expected that the compounds of general structure I taught by Ishida et. al., which encompasses analogs of Centaureidin with an extra – OCH<sub>3</sub> group instead of an –OH group, and Centaureidin of the instant application, would have similar chemical, physical and biochemical properties.

The phrase: "whereby elongation of melanocytic dendrites is inhibited" is not given any patentable weight because: the whereby clause represents the intended result of the process steps positively recited. See MPEP 2111.04: In *Hoffer v.*

*Microsoft Corp.*, 405 F.3d 1326, 1329, 74 USPQ2d 1481, 1483 (Fed. Cir. 2005), the court held that when a “whereby” clause states a condition that is material to patentability; it cannot be ignored in order to change the substance of the invention.” *Id.* However, the court noted (quoting *Minton v. Nat’l Ass’n of Securities Dealers, Inc.*, 336 F.3d 1373, 1381, 67 USPQ2d 1614, 1620 (Fed. Cir. 2003)) that a “whereby clause in a method claim is not given weight when it simply expresses the intended result of a process step positively recited.” *Id.*

Alternatively, even if one were to give some weight to the phrase: “whereby elongation of melanocytic dendrites is inhibited”, naturally flows from the teachings of the prior art and will necessary be present in the method made obvious by Ishida, since Ishida teaches similar active steps of the instant application: applying compounds close related to Centaureidin to the skin of individuals in need of skin whitening. In other words, products of identical or similar composition cannot exert mutually exclusive properties when administered under the same circumstances. In other words, even though the prior art is silent regarding “*inhibiting elongation of melanocytic dendrites*”, by practicing the method made obvious by the prior art: “*applying compounds like Centaureidin to the skin*”, one will be also be “*inhibiting elongation of melanocytic dendrites*”, even though the prior art was not aware of it. Apparently, Applicant has discovered a new property or advantage of the method made obvious by the prior art. MPEP 2145 II states: “The fact that Applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art, cannot be the basis

for patentability when the differences would otherwise be obvious" *Ex parte Obiaya*, 227 USPQ 58, 60.

Since Ishida et. al. teach a method of skin whitening with compounds of formula I (see above), and since dyschromatosis is a disease associated with anomalous darkening of the skin, and since Centaureidin, which differs from those compounds by just one methyl group is expected to have similar chemical and biological properties, at the time of the invention it would have been *prima facie* obvious for a person of ordinary skill in the art to substitute one functional equivalence (a compound of formula I or structurally related to formula I) for another (Centaureidin) with an expectation of success, since the prior art establishes that both function in similar manner, thus resulting in the practice of claims 14, with a reasonable expectation of success.

Claim 16 is a narrower version of claim 14, which insofar recites the same limitations as claim 14, wherein a skin preparation for external use comprising 0.005 to 5% by weight of Centaureidin is applied.

Claim 17, further limits claim 16, wherein the skin preparation for external use is a cosmetic.

For claims 16 and 17, Ishida further teaches: that the cosmetic composition (cosmetic compositions are for external use) of the present invention includes 0.00005 to 10% by weight of the compounds of formula I (see page 2, paragraph [0007]). These percentages clearly overlap with the percentages of the instant claims.

Ishida does not teach the exact same percentages of the instant claims. However, MPEP 2144.05 states: In the case where the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a *prima facie* case of obviousness exists. *In re Wertheim*, 541 F.2d 257, 191 USPQ 90 (CCPA 1976); *In re Woodruff*, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990). Thus resulting in the practice of claims 16-17 with a reasonable expectation of success.

#### **(10) Response to Argument**

##### First, Appellant argues:

Claim 7 on Appeal is directed to applying Centaureidin to "skin of an individual in need of skin whitening, whereby elongation of melanocytic dendrites is inhibited". The Examiner erred in not giving this recited limitation patentable weight. A similar limitation is found in each of claims 12, 14, and 16. The Federal Circuit in *Jansen v. Rexall Sundown, Inc.* (342 F.3d 1329 (Fed. Cir. 2003); (Exhibit A; copy provided as Attachment A to the Response filed October 28, 2008) has ruled that the phrase "an individual in need thereof" must be accorded weight in determination of patentability.

##### The Examiner disagrees:

The phrase: "whereby elongation of melanocytic dendrites is inhibited" was given patentability weight, see above rejection where it states: "Alternatively, even if one were to give some weight to the phrase: 'whereby elongation of melanocytic dendrites is inhibited', naturally flows from the teachings of the prior art and will necessary be

*present in the method made obvious by Ishida, since Ishida teaches similar active steps of the instant application: applying compounds close related to Centaureidin to the skin of individuals in need of skin whitening”.*

Having said that, Applicant is further reminded that the phrase: “whereby elongation of melanocytic dendrites is inhibited” was initially not given any patentable weight because: the whereby clause represents the intended result of the process steps positively recited. See MPEP 2111.04: In *Hoffer v. Microsoft Corp.*, 405 F.3d 1326, 1329, 74 USPQ2d 1481, 1483 (Fed. Cir. 2005), the court held that when a “whereby” clause states a condition that is material to patentability; it cannot be ignored in order to change the substance of the invention.” *Id.* However, the court noted (quoting *Minton v. Nat 'l Ass 'n of Securities Dealers, Inc.*, 336 F.3d 1373, 1381, 67 USPQ2d 1614, 1620 (Fed. Cir. 2003)) that a “whereby clause in a method claim is not given weight when it simply expresses the intended result of a process step positively recited.” *Id.* (Emphasis added). As such, The whereby clause, as recited in the present claims has not been given any patentable weight since it simply expresses the intended result (inhibition of melanocytic dendrites) of process steps positively recited ( administration of compounds structurally similar to Centaureidin to individuals in need of skin whitening).

Second, Appellant argues:

Although Centaureidin and the compounds of formula I disclosed by Ishida are structurally similar, they have different mechanism of action: Centaureidin inhibits length of dendrites, while the compounds of formula I disclosed by Ishida inhibit the production

of melanin. Applicant provides evidence that shows that the mechanism of action of Centaureidin and Nobiletin (a compound encompassed by the formula I of Ishida, see structure III on page 3 of Ishida) are different (see Exhibits C and D).

For this reason, Centaureidin can treat skin discoloration that cannot be treated by the compounds of Ishida, and as such the patient population being treated by Centaureidin is different than the patient population that can be effectively treated with the compounds disclosed by Ishida. Specifically, the compounds of Ishida will have minimal effect on dyschromatosis, as opposed to Centaureidin which is effective in treating dyschromatosis.

Exhibit B shows the general knowledge in the prior art that melanin granules are produced by melanocytes in the basal epidermal layer, and then these melanin granules are transferred to keratinocytes by elongation of melanocytes dendrites.

The effective concentration of Centaureidin required to inhibit the elongation of melanocytic dendrites is much less than the effective concentration of Nobiletin (a compound encompassed by the formula I of Ishida, see structure III on page 3 of Ishida) to inhibit the production of melanin granules. Referring to the 1st Tada Declaration (Exhibit C) the Declaration shows that  $10^{-5}$  % Centaureidin is effective to inhibit the elongation of melanocytic dendrites.  $10^{-5}$  % of Centaureidin corresponds to about 0.27  $\mu\text{M}$ . On the other hand, as show in the 2nd Tada Declaration (Exhibit D), the effective concentration of Nobiletin to inhibit the production of melanin granules is more than 1  $\mu\text{M}$ .

As discussed above, the effects of Centaureidin and Nobiletin (as taught by Ishida, et al.) are clearly different from each other. Although Centaureidin and Nobiletin are structurally similar to each other, the effectiveness observed with Centaureidin in inhibition of pigmented spot or dark complexion is not obtained using Nobiletin. This result cannot be derived from Ishida, et al. and is unexpected.

The claims on appeal are directed to treatment of different conditions that taught by Ishida

Ishida is directed to treatment of conditions caused by melanin overproduction. Appellants' claimed invention is directed to treatment of conditions caused by elongation of melanocytic dendrites. While both treatments relate to skin, the two treatments are not interchangeable as some skin conditions result from elongation of melanocytic dendrites rather than melanin production. Accordingly, the reasons for the similar symptoms are different and require different treatment.

Conclusion: In view of the foregoing arguments distinguishing Claims 7, 12-14 and 16-17 over the prior art, Appellant respectfully requests that the rejection of these claims be reversed.

The Examiner disagrees:

It is not clear from the way that the instant claims are constructed, that the patient population is actually limited by the phrase "whereby elongation of melanocytic dendrites is inhibited". It seems that this phrase ("whereby elongation of melanocytic dendrites is inhibited") is referring to an action that occurs as a consequence of



administering Centaureidin to individuals in need of skin whitening, and not that Centaureidin is administered to individuals in need of skin whitening and "in need of inhibition of elongation of melanocytic dendrites". As such, the claims are made obvious by the teachings of Ishida, since Ishida teaches the treatment of skin darkening comprising the administration of compounds of formula I, and as such the skilled in the art will be able to modify the general structure of formula I in order to make a series of similar compounds that will encompass Centaureidin, thus resulting in the practice of the instant claims with a reasonable expectation of success.

As such, the phrase: "whereby elongation of melanocytic dendrites is inhibited" is not given any patentable weight because: the whereby clause represents the intended result (i.e. elongation of melanocytic dendrites) of the process steps positively recited (Applying Centaureidin to the skin of an individual in need of skin whitening). See MPEP 2111.04: In *Hoffer v. Microsoft Corp.*, 405 F.3d 1326, 1329, 74 USPQ2d 1481, 1483 (Fed. Cir. 2005), the court held that when a "whereby" clause states a condition that is material to patentability; it cannot be ignored in order to change the substance of the invention." *Id.* However, the court noted (quoting *Minton v. Nat'l Ass'n of Securities Dealers, Inc.*, 336 F.3d 1373, 1381, 67 USPQ2d 1614, 1620 (Fed. Cir. 2003)) that a "whereby clause in a method claim is not given weight when it simply expresses the intended result of a process step positively recited." *Id.*

**(11) Related Proceeding(s) Appendix**

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

/MARCOS SZNAIDMAN/

Examiner, Art Unit 1628

Conferees:

/Frederick Krass/

Supervisory Patent Examiner, Art Unit 1612

/Brandon J Fetterolf/

Supervisory Patent Examiner, Art Unit 1628